said product can be, directly or indirectly, detected; and

the reporter gene is in operative association with said transcriptional control element; and

the cells express a nicotinic acetylcholine receptor that contains one or more subunits encoded by the nucleic acids.

93. (Amended) The method of claim 92, wherein, prior to comparing the difference in the amount of transcription, the cells [of claim 91] are contacted with a nicotinic acetylcholine receptor agonist.

REMARKS

A Petition for extension of time for three months and a check for the requisite fee for the extension and for a terminal disclaimer. Any fees, including those for the extension of time, the terminal disclaimer and any additional claims, that may be due may be charged to Deposit Account No. 02-4070. If the Petition for extension of time is absent, this paper is to be considered such Petition.

A terminal disclaimer accompanies this response.

Claims 53, 55-63, 66-68 and 70-74, 76, 77 and 79-99 are presently pending in this application. Claims 79, 81 and 85 are allowed, and claims 73 and 94 are objected to. Claims 53, 55-63, 66-68, 71, 72, 76, 77, 82-84 and 91-93 have been amended and claims 97-99 have been added in order to more particularly point out and distinctly claim the subject matter that applicant regards as the invention. The amendments and new claims primarily change the form, not the substance, of the claimed subject matter. Claim 54, 75 and 78 have been cancelled without prejudiced. As requested claim 75 has been cancelled as rewritten as a new claim. Claim 78, which depends upon claim 75, was cancelled and rewritten as claim 98 to avoid having a lower numbered claim depend from a higher numbered claim.

CORRECTION OF THE FILING RECEIPT AND FILING DATE OF THE APPLICATION AS ENTERED INTO THE PALM SYSTEM

It is respectfully submitted that the filing date of the above-captioned application was incorrectly entered into the PALM system as April 3, 1991. April 3, 1991 is the International filing date of this application. The 35 U.S.C. §102(e) date of this application should be the date of completion of the requirements for entering the National Stage in the U.S., which was November 30, 1992.

Attention is directed to the Decision on the Petition, under 37 C.F.R. §1.181, dated January 7, 1997. This Decision dismissed the Petition as unnecessary because the Petition Under 37 C.F.R. §1.181, dated February 22, 1994, granted the application the correct filing date of November 30, 1992. In that paper, it indicated that the case was being forwarded to Applications Division so that a corrected filing receipt would be issued. A new filing receipt was issued, but the date is again incorrectly entered as April 3, 1991.

The Decision on Petition Under 37 C.F.R. §1.181, dated February 22, 1994, page 2, states under the heading "Conclusion" that this application will be given a date of 30 November 1992 under 35 U.S.C. §371(c) and 102(e).

Applicant, therefore, after several failed attempts, respectfully requests the aid of the Examiner in obtaining corrected filing receipt that reflects the correct national stage filing date.

THE OBJECTION TO CLAIMS 93 and 94

Claims 93 and 94 are objected to being improperly dependent claims. Amendment of claim 93 obviates this inadvertent error. As amended claim 93 properly depends from claim 92.

THE REJECTION FOR OBVIOUSNESS-TYPE DOUBLE PATENTING

Claims 52, 54, 57-63, 66, 67, 74, 89 and 91 are rejected under the judicially created doctrine of obviousness-type double patenting. It is respectfully submitted that the Terminal Disclaimer filed herewith obviates this ground for rejection.

THE REJECTION OF CLAIMS 54-57, 58-63, 66-68, 70, 72-74, 76, 77, 86-92 AND 95 UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 54-57, 58-63, 66-68, 70, 72-74, 76, 77, 86-92 and 95 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that applicant regards as the invention. The various bases for this rejection are discussed in turn below. Reconsideration of the grounds for this rejection is respectfully requested in view of the amendments herein and the following remarks.

Relevant law

35 U.S.C. §112, second paragraph requires only reasonable precision in delineating the bounds of the claimed invention. The claim language is satisfactory if it reasonably apprises those of skill in the art of the bounds of the claimed invention and is as precise as the subject matter permits. Shatterproof Glass Corp.v. Libby-Owens Ford Col, 758 F.2d 613, 624, 225 USPQ 634, 641 (Fed. Cir), cert dismissed, 106 S. Ct. 340 (1985).

The amount of detail required to be included in the claims depends on the particular invention and the prior art and is not to be viewed in the abstract, but in conjunction with whether the specification is in compliance with the first paragraph of 35 U.S.C. §112. If the claims, read in light of the specification, reasonably apprise those skilled in the art both of the utilization and scope of the invention, and if the language is as precise as the subject matter permits, the courts can demand no more. Scripps Clinic & Research Foundation v. Genentech Inc. 18 USPQ 1001 CAFC 1991).

a) Claims 53, 54 and 58

Claims 53, 54 and 58 are rejected as allegedly reciting an improper Markush group. As amended the claims are not Markush claims, but rather recite each subunit as an alternative. "Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims." [see MPEP 2173.05(h), see also, In re Wolfrum 486 F.2d. 588, 179 USPQ 620 (CCPA 1971), which held that Section 112 cannot serve as the basis for rejecting a single claim on the ground that it embodies more than one invention (i.e., alternative)]. A Markush group is just one type of alternative form of expression. The alternatives set forth in the instant claims are not intended to be a Markush group. MPEP 2173.01 states:

> A fundamental principle contained in 35 U.S.C. 112, second paragraph is that applicants are their own lexicographers. They can define in the claims what they regard as their invention essentially in whatever terms they choose so long as the terms are not used in ways that are contrary to accepted meanings in the art. Applicant may use functional language, alternative expressions, negative limitations, or any style of expression or format of claim which makes clear the boundaries of the subject matter for which protection is sought. As noted by the Court in In re Swinehart, 439 F.2d 210. 160 USPQ 226 (CCPA 1971), a claim may not be rejected solely because of the type of language used to define the subject matter for which patent protection is sought.

Thus, a claim reciting alternative expressions is acceptable as it is unambiguous. In this instance, there is not ambiguity.

b) Claims 55-57

Claims 55-57 are alleged to be improperly dependent because there is not antecedent basis for "receptor encoded by . . . . claim 53". This language, however, does not refer to the a description of the nucleic acid, but rather refers to the subunit. Thus, the claims are directed to a "subunit of a neuronal nicotinic acetylcholine receptor". In the interests of advancing prosecution, however, the claims have been amended to recite a "human neuronal nicotinic acetylcholine receptor subunit", thereby eliminating any possible ambiguity.

c) Claim 57

Claim 57 is also rejected because a nucleic acid cannot hybridize to a nucleic acid sequence. Claim 57, however, did not recite a nucleic acid sequence, but rather recited a "sequence of nucleotides"; nucleotides are material entities. DNA can hybridize to nucleotides. Again in the interest of advancing prosecution, this claim has been amended by deleting the word "sequence", thereby obviating this rejection.

d) Claim 59

Claim 59 is rejected as being indefinite in failing to provide antecedent basis for "nucleic acids". Applicant respectfully disagrees. Claim 59 recites one or more", which can require a plural, and claim 53 sets forth three or alternative nucleic acids. Thus, there is antecedent basis for "nucleic acids". Recitation of "one or more nucleic acid of claim 53" does not render the claim more clear. As noted above, claim language is satisfactory if it reasonably apprises those of skill in the art of the bounds of the claimed invention and is as precise as the subject matter permits. Shatterproof Glass Corp.v. Libby-Owens Ford Col, 758 F.2d 613, 624, 225 USPQ 634, 641 (Fed. Cir), cert dismissed, 106 S. Ct. 340 (1985).

e) Claims 67 and 70

Claims 67 and 70 are rejected as being indefinite in failing to provide antecedent basis for "the" alpha 2, alpha 3 and beta 2 subunit. Applicant respectfully disagrees. Antecedent basis is provided in claim 59, which recites that the cells contain DNA encoding one or more of these subunits. As noted above, claim language is satisfactory if it reasonably apprises those of skill in the art of the bounds of the claimed invention and is as precise as the subject matter permits. Shatterproof Glass Corp.v. Libby-Owens Ford Col, 758 F.2d 613, 624, 225 USPQ 634, 641 (Fed. Cir), cert dismissed, 106 S. Ct. 340 (1985).

In the interest of advancing prosecution, however, "the" has been replaced with "a" or "an" in each instance.

f) Claim 68

Claim 68 is rejected in that it recites "electrophysiological response of the cells" twice. Claim 68 has been amended to correct this inadvertent error.

e) Claims 73, 74 and 86

Claims 73, 74 and 86 are rejected because the language "substantial homology" is allegedly indefinite because it has no clear meaning in the art. No evidence to support this assertion is provided. Applicant respectfully disagrees.

First it is respectfully noted that claims are read in light of the specification and the term "substantial" is only if definite if the specification does not provide a standard for measuring the degree intended:

> The phrases "relatively shallow," "of the order of," "the order of about 5 mm," and "substantial portion" were held to be indefinite because the specification lacked some standard for measuring the degree intended and, therefore, properly rejected as indefinite under 35 U.S.C. 112, second paragraph. Ex parte Oetiker, 23 USPQ2d 641 (Bd. Pat. App & Inter. 1992).

In this instance, however, the specification does provide a definition (see page 12, lines 16-33):

> Use of the phrase "substantial sequence homology" in the present specification and claims means that DNA, RNA or amino acid sequences which have slight and non-consequential sequence variations form the actual sequences disclosed and claimed herein are considered to be equivalent to the sequences of the present invention, and as such are within the scope of the appended claims. In this regard, "slight and non-consequential sequence variations" mean that "homologous" sequences (*i.e.*, the sequences that have substantial sequence homology with the DNA, RNA, or proteins disclosed and claimed herein) will be functionally equivalent to the sequences disclosed and claimed in the present invention. Functionally equivalent sequences will function in substantially the same manner to produce substantially the same compositions as the nucleic acid and amino acid compositions disclosed and claimed herein.

Thus it is clear what is intended by the term "substantial homology".

Second, the term substantial homology has an art recognized meaning. A search of the LEXPAT database revealed countless instances in which the term is defined in a manner similar to that set forth above. Furthermore, a search of the claims yielded 63 patents in which the term "substantial homology" or substantially homologous is set forth in a claim. These patents include U.S. Patent Nos. 4,511,652, 4,751,081, 4,766,073, 4,769,328, 4,798,885, 4,801,541, 4,801,542, 4,849,407, 4,886,754, 4,889,802, 4,894,333, 4,908,203, 4,918,006, 4,918,166, 4,933,288, 4,940,840, 4,952,499, 4,971,952, 5,008,240, 5,013,644, 5,023,078, 5,034,323, 5,045,471, 5,084,390, 5,124,255, in which this term is used to define the relationship between nucleic acid molecules or between proteins.

The fact that this language appears in claims in patents that issued prior to the filing date or around the time of the filing date of the instant application evidences that those of skill in the art would understand the language in the claim.

The caselaw holds that the use "substantially" is not of itself fatal. Eibel Process Co. v. Minnesota & Ontario Paper Co., 261 U.S. 45, 67 L. Ed. 523, 43 S. Ct. 322 (1923); use of "substantial" to describe an angle of pitch of a paper-making machine was sufficiently definite on the ground that those skilled in the art would know what was meant).

> indeed, it must always be implied in every claims, even when not introduced, and adds nothing when it is. Were this not true, few patents could be given any protection, for some departures from the precise disclosure are nearly always possible without losing the benefit of the invention. Musher Foundation v. Alba Trading Co., 150 F.2d 885, 66 USPQ 183 (2d Cir. 1945), cert. denied, 326 U.S. 770 (1945).

THE REJECTION OF CLAIMS 54-57, 58-63, 66-68, 70, 72-74, 76, 77, 86-92 AND 95 UNDER 35 U.S.C. §112, FOURTH PARAGRAPH

Claims 55, 56, 68, 72, 76-78, 82-84 and 92 are rejected under 35 U.S.C. 112, fourth paragraph, as being improperly dependent for allegedly failing to limit the claim upon which each depends. Applicant respectfully traverses this rejection. Although applicant disagrees with the propriety of this rejection (see, discussion below and MPEP 608.01(n)], in the interest of advancing prosection, claims 68, 72, and 92 have been amended. This rejection is rendered moot with respect to claims 68, 72 and 92 and also with respect to claims 55 and 56.

First it is noted that claims 55 and 56 as amended are not identical. Claims 68, 72 and 92 as amended are independent claims. It is noted, however, that the claim structure of these claims prior to amendment was proper.

The test as to whether a claim is a proper dependent claim is that:

> . . . it shall include every limitation of the claim from which it depends (35 U.S.C. 112, fourth paragraph) or in other words that it shall not conceivably be infringed by anything which would not also infringe the basic claim.

> A dependent claim does not lack compliance with 35 U.S.C. 112, fourth paragraph, simply because there is a question as to (1) the significance of the further limitation added by the dependent claim, or (2) whether the further limitation in fact changes the scope of the dependent claim from that of the claim from which it depends. The test for a proper dependent claim under the fourth paragraph of 35 U.S.C. 112 is whether the dependent claim includes every limitation of the claim from which it depends. *The test is not one of whether the claims differ in scope.* [emphasis added, see MPEP 608.01(n)].

Thus, claims 55, 56, 76 to 78 and 82-84 are properly dependent because each of these claims "includes every limitation of the claim from which it [each] depends".

Finally it is noted, that this application is the national stage of an international PCT application. Where national and international rules conflict, international rules should apply. In international practice dependent claims are preferred over independent claims.

THE REJECTION OF CLAIM 80 UNDER 35 U.S.C. §101

Claim 80 is rejected under 35 U.S.C. §101 for statutory double patenting as claiming the same invention as claim 1 of U.S. Patent No. 5,369,028. This rejection is respectfully traversed. It is respectfully submitted that claim 80 and claim 1 of the patent are not of the same scope and thus do not claim the same invention.

Statutory double patenting under 35 U.S.C. §101 exists when two or more patents are granted that contain claims that encompass the same inventive concept. In order for such a rejection to be proper, the claims of both applications must be of the same scope. The test for double patenting under 35 U.S.C. §101 is whether it is possible to infringe the claims of one application without infringing the claims of the other application. If it is possible to infringe the claims of one application and not the other, the claims are of different scope.

Claim 80 recites:

80. Isolated nucleic acid of claim 57, comprising the alpha3-encoding nucleic acid that is isolated from a plasmid having all of the identifying characteristics of HnAChRα3 deposited under ATCC Accession No. 68278.

Claim 1 of U.S. Patent No. 5,369,028 recites:

1. Isolated and purified DNA consisting of the human neuronal nicotinic acetylcholine receptor alpha3 subunit-encoding portion of plasmid HnAChRα3 (ATCC Accession No. 68278), and degenerate variants thereof.

In this instance it is possible to infringe the claims of this application without infringing the claims of U.S. Claim 80 recites a "nucleic acid, comprising . . ." ; whereas claim 1 of the patent "DNA consisting of".

Comprising is open language. As a result this claim will be infringed by any nucleic acid that comprises the alpha3-encoding nucleic acid; whereas a nucleic acid that comprises the alpha3-encoding nucleic acid would not literally infringe claim 1 of the patent. Also, claim 80 is directed to nucleic acid, which includes DNA and RNA; whereas claim 1 of the patent recites DNA. Claim 80 will be infringed, for example, by mRNA comprising the recited sequence; whereas claim 1 will not be literally infringed by such mRNA.

Therefore, as between claim 1 of the patent and claim 80 of the instant application, statutory double patenting does not exist. Any issues that would arise under the doctrine of obviousness-type double patenting will be rendered moot by virtue of the terminal disclaimer filed herewith.

THE REJECTION OF CLAIMS 53-63, 66-68 and 70-75 UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 53-63, 66-68 and 70-77, 86, 88-92, 95 and 96 are rejected under 35 U.S.C. §112, first paragraph, because the disclosure is allegedly only enabling for DNA encoding a neuronal nicotinic acetylcholine receptor encoded by any of the deposited plasmids. In particular, it is urged that:

> the disclosure is enabling only far claims limited to a nucleic acid encoding one of the subunits which is encoded by the biological material that was deposited

because:

> neither the amino acid sequence or any other structural information has been provided about this protein. The specification does not disclose how this clone was made and does not identify those parts of the protein encoded thereby which are essential for its biological activity. In the absence of this information a practitioner would be incapable of producing a human alpha2 nAchR subunit other than that which is encoded by this clone.

This rejection is respectfully traversed insofar as it applies to any of the presently pending claims.

The Examiner provides no reasons for concluding that the clones and sequences set forth in the application could not have been used to isolated substantially homologous nucleic acid. It is irrelevant whether or not the specification provides a detailed description of how the deposited clones were identified. The specification must teach one of skill in the art how to make and use what is claimed without undue experimentation. There is no requirement that the specification teach how the instant applicant achieved its particular result (unless there is evidence that the applicant believed that its way constitutes the best mode). Furthermore, in this instance, the specification does teach how these clones were identified and teaches that the isolated clones can be used to isolate related clones. Starting at page 12, about line 12, the specification teaches:

> by probing numerous human cDNA libraries, e.g., pre-frontal cortex cDNA, parietal cDNA, temporal cortex cDNA, brain stem cDNA, basal ganglia cDNA, and spinal cord cDNA, various fragments of the human neuronal subunits were identified (see, for example, Figures 4, 5 and 6). After partial sequencing and restriction mapping of several such fragments . . . it was possible to identify composite DNA sequences for the human neuronal alpha2, alpha3 and beta2 subunits, as disclosed and claimed herein.
>
> In addition to their use as coding sequences for the production of human neuronal subunits and synthetic human neuronal receptors, the invention sequences can also be used as probes for the identification of additional human neuronal sequences. This is done by probing various sources of human neuronal DNA with invention sequences, then selecting those sequences having a significant level of sequence homology with the probe employed.

Thus, the specification also teaches that the deposited clones can be used to isolate related clones.

Also, the specification does provide sequence information regarding DNA and, thus, the encoded proteins. Sequence ID Nos. 1, 3, 5, 7 and 9 set forth nucleic acid sequences for each of the subunits. The specification also provides restriction maps of the deposited clones. It would not require undue

experimentation to use the disclosed DNA and/or the deposited clones as probes to identify and isolate closely related (i.e., substantially homologous) DNA molecules.

Relevant law

In order to satisfy the enablement requirement of 35 U.S.C §112, first paragraph, the specification must teach one of skill in the art to make and use the invention without undue experimentation. Atlas Powder Co. v. E.I. DuPont de Nemours, 750 F.2d 1569, 224 USPQ 409. This requirement can be satisfied by providing sufficient disclosure, either through illustrative examples or terminology, to teach one of skill in the art how to make and how to use the claimed subject matter without undue experimentation. This clause does not require "a specific example of everything within the scope of a broad claim." In re Anderson, 176 USPQ 331, at 333 (CCPA 1973). Rather, the requirements of §112, first paragraph "can be fulfilled by the use of illustrative examples **or** by broad terminology." In re Marzocchi et al., 469 USPQ 367 (CCPA 1971), emphasis added.

Further, because "it is manifestly impracticable for an applicant who discloses a generic invention to give an example of every species falling within it, or even to name every such species, it is sufficient if the disclosure teaches those skilled in the art what the invention is and how to practice it." In re Grimme, Keil and Schmitz, 124 USPQ 449, 502 (CCPA 1960). Thus, there is no doubt that a patentee's invention may be broader than the particular embodiment shown in the specification. A patentee is not only entitled to narrow claims, particularly directed to the preferred embodiment, but also to broad claims that define the invention without a reference to specific instrumentalities. Smith v. Snow, 294 U.S. 1, 11, 24 USPQ 26, 30 (1935).

Thus, there is no requirement for disclosure of every species within a genus. Applicant is entitled to claims that are commensurate in scope not only with what applicant has specifically exemplified, but commensurate in scope with that which one of skill in the art could obtain by virtue of that which the applicant has disclosed.

The inquiry with respect to scope of enablement under 35 U.S.C. §112, first paragraph, is whether it would require undue experimentation to make and use the claimed invention. A considerable amount of experimentation is permissible, particularly if it is routine experimentation. The amount of experimentation that is permissible depends upon a number of factors, which include: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, and the breadth of the claims. Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int'f 1986); see also In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988).

A. It would not require undue experimentation to make and use the claimed DNA fragments and cells

As stated above, the inquiry with respect to scope of enablement under 35 U.S.C. §112, first paragraph, is whether it would require undue experimentation to make and use the claimed invention. A considerable amount of experimentation is permissible, particularly if it is routine experimentation. The amount of experimentation that is permissible depends upon a number of factors, which include: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, and the breadth of the claims. Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int'f 1986); see also In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988).

As discussed below the claims are commensurate in scope with the disclosure, which exemplifies particular embodiments within the scope of the claims and also teaches how one of skill can obtain other embodiments within the scope of the claims.

The level of skill in the art is high

The level of skill in this art is recognized to be high (see, e.g., Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int'f 1986)). In addition, the numerous articles and patents that are of record in this application that are authored by those of a high level of skill for an audience of a high level of skill further evidences the high level of skill in this art.

The scope of the claims

The claims encompass DNA that encodes the subunits encoded by the deposited clones or that have only minor sequence variations (or degenerate codons). The claims are limited to the specified subtypes and to minor variants thereof that fall within the definitions provided in the specification. In light of the limiting definition of each subunit, the functional language in the claims limiting each claim to DNA encoding each subunit or cells containing the DNA encoding the specified human neuronal nicotinic acetylcholine receptor subunits, the description of sequences of each subunit and the deposit of clones containing DNA encoding each subunit, as well as the high level of skill in the art. Only those DNA fragments that have are the same or have minor, inconsequential variations of the DNA fragments disclosed in the specification, such as degenerate codons, are encompassed by the instant claims.

Claims are intended to be read in light of the specification, thus the definition of substantial sequence homology, which refers to minor and inconsequential sequence variations, cannot be ignored. The claims simply do not encompass DNA encoding analogs of each subunit, but are intended to encompass the disclosed subunits or minor variants thereof.

The claims are limited to specific subtypes of α and β subunits. As disclosed in the specification, the sequences of α_3 and α_2 are homologous, but distinct subunits. So that, in reality the variability of sequence that is implicitly in the instant claims is very limited. If DNA is isolated that encodes an α or a β subunit that is different to any extent from the sequences disclosed in the application or the sequences of the deposited clone, such DNA encodes a distinct subunit and, thus, is not within the scope of the instant claims.

Therefore, the claims do not encompass innumerable fragments, insertions and rearrangements that read on unrelated proteins. The claims include two substantive limitations: 1) the DNA encodes either a human neuronal nicotinic acetylcholine receptor α_2, α_3 or β_2 subunit **and** 2) is substantially the same as or encodes the same amino acids as the sequence of the DNA set forth in the figures or deposited at the ATCC. Any DNA fragment that encodes an unrelated protein is not encompassed within the instant claims. Any DNA fragment that encodes even a different subtype of the same subunit, such as a β_3 subunit, is not encompassed within the claims [other than claim 53]. Further, unlike the claim at issue in Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., the claims do not encompass analogs of the subunits. Thus, the claims encompass the specifically disclosed DNA, the deposited DNA and DNA that can be constructed by substituting degenerate codons for the codons in the disclosed or deposited DNA, and DNA that encodes minor, but equivalent, amino acid alternations, such as DNA that encodes a protein that includes a single conservative amino acid change.

In addition, there is guidance presented in the specification for isolating DNA, there are deposited clones that comprise DNA that encodes all or a substantial portion (5 nucleotides are missing from the deposited α_2-encoding clone) of each subunit. Also, partial or complete sequences of each subunit are set forth in the specification.

Teaching and guidance in the specification

The specification teaches how to introduce the DNA encoding the subunits into host cells, express such DNA to produce functional heterologous nicotinic acetylcholine receptors and test such for activity. Thus, the specification provides sufficient guidance to permit those of skill in the art to ascertain whether a particular subunit encoded by DNA that is not identical to the deposited or disclosed DNA encodes a functional subunit.

Patents are written to enable those of skill in the art to practice the invention. A patent need not disclose what is well known in the art (W.L. Gore & Assoc. v. Gorlock, Inc., 721 F.2d 1540, 1556, 220 USPQ 303, 315). In this instance, those of skill in the art would have access to the deposited DNA and would be able, if necessary, to sequence the DNA encoding each subunit and/or to use the deposited clones to readily isolate other such clones.

The specification defines (page 11, lines 7-31) what is encompassed by the DNA encoding each subunit and defines substantial sequence homology. For example, the specification states that α_2 "refers to a gene, which has been identified in chick and rat, that encodes a neuronal subunit of the same name". In addition, the specification provides a partial DNA sequence of the α_2 subunit, a restriction map of the clone, and indicates that a plasmid encoding the α_2 has been deposited in a recognized depository. The α_3 and β_2 subunits are similarly defined. Further, the specification teaches that the both subunits are required for formation of a functional ligand-gated channel and defines substantial sequence homology to encompass only minor and inconsequential sequence variations. The specification teaches DNA encoding each of the subunits and provides deposits that contain this DNA and also, as discussed above, defines what is intended for each DNA clone encoding the each subunit to encompass.

One of skill in this art could readily obtain the deposited clones or obtain DNA having the sequence set forth in the figures and one of skill in this art could readily substitute degenerate codons for the codons set forth in the

figures or the codons in the deposited DNA. The DNA can be identified by comparison with the sequence of the disclosed or deposited DNA and by inclusion of an open reading frame that encodes one of the specified subunits. If necessary the DNA can be introduced into cells and used to produce functional receptors whose activity can be assessed as exemplified in the application.

Conclusion

Therefore, it would not require undue experimentation for one of skill in the art to make and use the claimed subject matter. Therefore in light of the instant specification, no undue experimentation is required to isolate DNA encoding the α_2, α_3 and β_2 subunits.

Furthermore, it is unfair and unduly limiting to require applicant to limit the claims to only the disclosed embodiment. To do so is contrary to the public policy upon which the U.S. patent laws are based. If applicant is required to limit the claims to only the DNA contained in the deposited plasmids, then those of skill in the art could by virtue of these deposits isolate DNA encoding closely related subunits or readily modify the disclosed DNA and practice what is disclosed in the application, but avoid infringing such limited claims. To permit that is simply not fair. The instant application teaches DNA encoding each of these subunits and thereby provides a means for others to isolate such subunits. As is apparent from the specification and the DECLARATION, this was clearly not a routine task, but required creative invention to have obtained the clones. Thereafter, having such clones, permits one of skill to readily isolate related clones. Thus, the disclosure and the deposits permit others to readily clone other such subunits or to make minor changes in deposited DNA and thereby avoid infringement.

Certainly, applicant is entitled to claims to the deposited plasmids and/or to the portion of each plasmid that comprises DNA that encodes all or a portion of a nicotinic acetylcholine receptor subunit and is entitled to claims that encompass the disclosed nucleic acid fragments. Applicant is the first to have isolated any human nicotinic acetylcholine receptor-encoding DNA, and as such should be entitled to claims directed thereto.

B. The instant claims are not analogous to claim 7 in U.S. Patent No. 4,703,008, which was deemed invalid under 35 U.S.C. §112, first paragraph, as not being enabled by the specification

First, it is noted that enablement is determined by reference to the teachings in the specification and the knowledge of those of skill in the art at the time of filing (such knowledge is presumed to be part of the application disclosure). Thus, a finding that a claim is of analogous scope to one deemed non-enabled in one case, has no relevance to the case at issue, since enablement is a function of the teachings in the specification. As discussed below (B), the instant specification teaches how to make and use what is claimed without undue experimentation.

Assuming, arguendo, that such determination is relevant, it is respectfully submitted that the instant claims are not analogous to claim 7 of U.S. Patent No. 4,703,008, but rather are more analogous to claim 2, which was deemed valid.

Briefly, Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 18 USPQ2d 1016, (CAFC 1991) (hereinafter, Amgen or Amgen v. Chugai) concerns the infringement and validity of two patents, U.S. Patent No. 4,703,008, assigned to Amgen, Inc. and U.S. Patent No. 4,677,195, assigned to Genetics Institute (hereinafter, the '008 and '195 patents, respectively). One of the court's considerations in this case was the validity of claims 2 and 7 of the '008. Claim 2 was challenged as obvious in view of the prior art and was

held valid by the court. Claim 7 was challenged as lacking enablement under 35 U.S.C. §112 and was held to be invalid by the court.

The claims at issue here are very different from the claim in the Amgen patent to which the Examiner refers. Claim 7 in U.S. Patent No. 4,703,008 reads:

> 7. A purified and isolated DNA sequence consisting essentially of a DNA sequence encoding a polypeptide having an amino acid sequence sufficiently duplicative of that of erythropoietin to allow possession of the biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells, and to increase hemoglobin synthesis or iron uptake.

Claim 7, thus, reads, not only on peptides encoding erythropoietin but also on other peptides, erythropoietin analogs, i.e. peptides with "EPO-like" activity (see, Amgen Inc. v. Chugai Pharmaceutical Co. Ltd. at 1028), that have a similar sequence such that they possess two biological properties in common with erythropoietin. The Court found that the claims encompass analogs of erythropoietin and that Amgen had failed to find any erythropoietin analogs that possess both requisite biological properties. In addition, the supporting language in the specification defined the DNA fragments to include any that hybridize; the language of the instant claims that is more limited and is not intended to encompass alpha2-like-, alpha3-like- and beta2-like-encoding DNA.

Thus, the claims are far more narrowly drawn than those at issue in Amgen Inc. v. Chugai Pharmaceutical Co. Ltd. and are more analogous to claim 2 of Amgen, which has been held valid. Claim 2 recites:

> A purified and isolated DNA sequence consisting essentially of a DNA sequence encoding erythropoietin.

In this instance, most of the claims at issue herein are more limited than claim 2 of Amgen, since the instant claims include sequence limitations and functional limitations. In addition, the instant specification provides for definitions of the intended scope of the claims. Also, claim 7 of patent at issue in Amgen defined the encoded DNA with reference to the biological activity of the

encoded protein; the specified biological activities do not necessarily uniquely define erythropoietin. Thus, the claim was held to encompass erythropoietin analogs.

With respect to invalidated claim 7, the court held that "it (was) not sufficient, having made the gene and a handful of analogs whose activity (had) not been clearly ascertained, to claim all possible genetic sequences that have EPO-like activity," Amgen v. Chugai, 18 USPQ2d 1016 at 1028, emphasis added. The court also states, however, that "[i]t is well established that a patent applicant is entitled to claim his invention generically, when he describes it sufficiently to meet the requirements of Section 112," directing attention to Utter v. Hiraga, 845 F.2d 993, 998, 6 USPQ2d 1709, 1714 (Fed. Cir. 1988); and In re Robins, 429 F.2d 452, 456-457, 166 USPQ 552, 555 (CCPA 1970). Thus, claim 2 of the '008 patent, directed to "DNA sequence consisting essentially of a DNA sequence encoding human erythropoietin," was properly enabled by the specification.

Furthermore, the specification defines all terms used in the claims and clearly sets forth the intended scope contemplated by each term. As established below, the claims do not encompass DNA encoding any and all such receptors but a clearly defined and readily obtainable subset thereof. Therefore, the specification is not comparable to that in U.S. Patent No. 4,703,008, in defining the intended scope of claim 7.

As noted above, the instant claims are more narrowly drawn than that at issue in Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.. First, the instant claims are limited to DNA encoding the **human** neuronal NAChR α_2, α_3 or β_2 subunits and to cells containing the DNA. Thus, the claims are limited to DNA encoding particular subtypes of each receptor subunit. The DNA includes DNA having substantially the same sequence as the deposited DNA and DNA that encodes subunits that have substantially the same sequence as the subunits encoded by

the deposited plasmids or that encode proteins that include the sequences of amino acids set forth in the figures.

THE REJECTION OF CLAIMS 55, 56, 76-78 and 82-84 UNDER 35 U.S.C. §102(B)

Claims 55, 56, 76-78 and 82-84 are rejected under 35 U.S.C. §102(b) as being clearly anticipated by Whiting et al. because the limitation "substantially pure" allegedly only requires any state of purity that is higher than that which occurs in nature. This rejection is respectfully traversed.

Applicant respectfully disagrees with the assertion that "substantially pure" allegedly only requires any state of purity that is higher than that which occurs in nature. No basis for this conclusion is provided.

In the interests of advancing prosecution of this application, the claims have been amended to result "isolated", thereby rendering this ground of rejection moot.

* * *

In view of the above amendments and remarks, reconsideration and allowance of the application are respectfully requested.

Respectfully submitted,
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